UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,833	06/16/2006	David Durantel	P08599US00/BAS	3759

881 7590 06/03/2010

STITES & HARBISON PLLC
1199 NORTH FAIRFAX STREET
SUITE 900
ALEXANDRIA, VA 22314

EXAMINER	
WOOLWINE, SAMUEL C	
ART UNIT	PAPER NUMBER
1637	
MAIL DATE	DELIVERY MODE
06/03/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,833	DURANTEL ET AL.	
	Examiner	Art Unit	
	SAMUEL C. WOOLWINE	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2009 and 28 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28 and 31-78* is/are pending in the application.

4a) Of the above claim(s) *31-76* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28 and 37-78* is/are rejected.

7)☒ Claim(s) *9,10,14,16,52,53,57 and 59* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 December 2008* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Office action mailed 05/11/2010 is hereby withdrawn to be superseded by this Office action, which addresses new issues not raised in the 05/11/2010 Office action. This sets a new time period for response from Applicant. The contents of the previous Office action are reiterated here. Therefore, Applicant need only respond to this Office action and not the one mailed 05/11/2010.

Status

Applicant's reply submitted 10/23/2009 is acknowledged.

Claims 1-28 and 31-78 are pending in the application. Claims 31-36 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 06/03/2008.

The Sequence Compliance issues raised in the Office action mailed 04/24/2009 (OA 04/24/09) are resolved by Applicant's submission of revised sequence listing and amendments to the specification. In addition, the sequence issues raised in the notice mailed 12/30/2009 have been corrected by Applicant's submission of a corrected sequence listing on 01/28/2010.

The replacement drawings submitted 10/23/2009 for figures 1-4 are accepted; the objections to the drawings raised in OA 04/24/09 are withdrawn. The objections to the claims for reciting non-elected SEQ ID NOs raised in OA 04/24/09 are withdrawn; this objection was made in error.

The rejections made under 35 USC 112, 2nd paragraph in OA 04/24/2009 are withdrawn in view of Applicant's amendments.

Claims 1-28 and 37-78 require one or both of primers SEQ ID NO:17 and SEQ ID NO:18. These primer sequences are free of the prior art. Each of these primers was designed by Applicant from known HBV sequence, and then altered so as to create a restriction site (SphI or SalI) internally in the primer (see pages 13-14 of the specification as filed). That is, the first 6 or so nucleotides and last 19 or so nucleotides match HBV genomic sequence, with the 5 or so nucleotides in-between altered from the HBV sequence so as to create the restriction site for the purpose of cloning the resulting fragment into a vector. While it was known in the art to add a restriction site to the 5' end of a primer to facilitate cloning of the resulting PCR product, and while it was also known in the art to add one or more additional bases at the 5' end to facilitate the cutting of the PCR product by the restriction enzyme, there was no apparent reason why one would have created such a site internally within a 30-mer sequence instead of just adding the restriction enzyme site (and additional arbitrary bases to aid in cutting by the restriction enzyme) at the 5' end. That is, the inclusion of CTAAGG at the 5' end of SEQ ID NOs 17 and 18 was not obvious.

Nevertheless, while the claims have been found free of the art, the examiner has set forth some new rejections under 35 USC 112, 2nd paragraph below, as well as reiterated an earlier objection to a drawing that was not clearly addressed. While, ordinarily, the examiner would attempt to resolve the section 112 issues by telephonic

interview and examiner amendment, the examiner cannot resolve the problem with the drawings. Therefore, this Office action will be mailed and is NON-FINAL.

Drawings

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because the replacement for figure 7, submitted on 12/22/2008, is not legible. First, the text is too small. See 37 CFR 1.84(p)(3): "Numbers, letters, and reference characters must measure at least.32 cm. (1 /8 inch) in height." Second, the figure legend for the graph appears to indicate 5 data series (plotted lines), but only 3 are visible in the graph. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Objections

Claims 9, 10, 14, 16, 52, 53, 57 and 59 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. These claims differ from the claims from which they depend (claims 8, 5, 11, 15, 51, 48, 54 and 58, respectively) only in specifying that the forward/reverse primer of the first/second primer pair comprises a sequence selected from particular SEQ ID NOs. However, all these claims depend ultimately from claim 1, which already specifies these limitations (i.e. that the forward/reverse primer of the first/second primer pair comprises

a sequence selected from these particular SEQ ID NOs). Hence, claims 9, 10, 14, 16, 52, 53, 57 and 59 are not seen as further limiting.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-28 and 37-78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (steps a and b) recites the phrase "transcriptable in pgRNA". It is vague and indefinite what this phrase means. The examiner presumes that it means "capable of being transcribed to produce HBV pgRNA", and such language would be more favorably considered. As all claims ultimately depend from claim 1, they are rejected for the same reason.

In addition, claims 2 and 45 recite "an about 1 genome unit starting in 5' from...". It is unclear what "in 5' from" means. The language "5' of" would be more favorably considered. Likewise, in the phrase "to the first nucleotide in 5' of the ATG...", the meaning of "in 5' of" is unclear. The language "5' of" would be more favorably considered. In addition, reference to "the ATG of the pre-C" gene is vague and indefinite, since it is not specified *which* ATG of the pre-C gene is intended. Presumably "the ATG start codon of the pre-C gene" is intended, and this language would be more favorably considered.

With regard to claims 3, 4, 46 and 47, the claims are vague and indefinite because the claim requires one to know the identity of nucleotides 1818-1813 and 1814-1960 (in the case of claims 3 and 46) or nucleotides 1816-1813 and 1814-2016 (in the case of claims 4 and 47) of an undisclosed HBV genomic sequence. Based on the "alignment" language, Applicant apparently intends to indicate the regions corresponding to those in the GenBank sequence. However, the language of the claim clearly indicates particular nucleotide sequences of "an HBV genomic sequence", not those of the GenBank sequence. The problem is that, when one aligns an HBV genome sequence with the GenBank sequence, the positions may not correspond numerically. For example, a particular (perhaps newly discovered) HBV sequence may be longer or shorter than the GenBank sequence, and so position 1818 of the "new" HBV sequence may not be lined up with position 1818 of the GenBank sequence when the two sequences are aligned. This is important because Applicant's method is based on amplifying two fragments of the HBV genome, with each fragment including or excluding certain features (e.g. transcription start site, ATG start codon of pre-C gene, etc). The examiner would propose the following language (for example, for claim 3): "The method according to claim 2, wherein the continuous DNA sequence comprises from 5' to 3' nucleotides of an HBV genomic sequence corresponding to nucleotides 1818 to 1813 and 1814 to 1960 of GenBank sequence GI 13365548 when said HBV genomic sequence is aligned with said GenBank sequence. " It is believed that this is what Applicant intended to convey.

Likewise, in claims 6 and 49, reference to "the ATG of the pre-C" gene is vague and indefinite, since it is not specified *which* ATG of the pre-C gene is intended. Presumably "the ATG start codon of the pre-C gene" is intended, and this language would be more favorably considered.

In addition, in claims 11 and 54, the phrase "in 5' with respect to" is unclear. The language "5' with respect to" would be more favorably considered.

In addition, in claims 15 and 58, the phrase "in 3' of" is unclear. The language "3' of" would be more favorably considered.

Claims 20 and 63 recite that the "heterologous promoter is fused to the +1 of transcription of the HBV fragment", referring back to claim 1 (or 43, which itself depends from claim 1). However, claim 1 discloses two HBV fragments, so it is unclear which fragment is being referred to in claim 20. Presumably, Applicant means that the heterologous promoter "is fused to the +1 of transcription of the HBV pgRNA encoded by the linear continuous DNA sequence", and such language would be more favorably considered.

With regard to claim 42, the phrase "determination of the incidence of the pharmaceutical product on viral gene expression and/or replication" is unclear, since the term "incidence" in this context is confusing. The term "effect", as opposed to "incidence", would be more favorably considered.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

> art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 4, 46 and 47 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. Information critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

Claims 3, 4, 46 and 47 recite that the continuous DNA sequence comprises, from 5' to 3', nucleotides corresponding to certain positions of GenBank GI Number 13365548. Note that MPEP 2422.03 states (emphasis provided by examiner):

> In those instances in which prior art sequences are only referred to in a given application by name and a publication or accession reference, they need not be included as part of the "Sequence Listing," unless an examiner considers the referred- to sequence to be "essential material," per MPEP § 608.01(p).

MPEP 608.01(p) states (emphasis provided by examiner):

> An application as filed must be complete in itself in order to comply with 35 U.S.C. 112. Material nevertheless may be incorporated by reference, *Ex parte Schwarze*, 151 USPQ 426 (Bd. App. 1966). An application for a patent when filed may incorporate "essential material" by reference to (1) a U.S. patent, or (2) a U.S. patent application publication, which patent or patent application publication does not itself incorporate such essential material by reference. See 37 CFR 1.57(c). Prior to October 21, 2004, Office policy also permitted incorporation by reference to a pending U.S. application.
>
> "Essential material" is defined in 37 CFR 1.57(c) as that which is necessary to (1) provide a written description of the claimed invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and set forth the best mode contemplated by the inventor of carrying out the invention as required by the first paragraph of 35 U.S.C. 112, (2) describe the claimed invention in terms that particularly point out and distinctly claim the invention as required by the second paragraph of 35 U.S.C. 112, or (3) describe the structure, material, or acts that correspond to a claimed means or step for performing a specified function as required by the sixth paragraph of 35 U.S.C. 112.

The sequence disclosed in GenBank GI: 13365548 referred to in the claims clearly represents essential material, since the claims cannot be understood without this information. For this, one needs to go outside of the application to understand the

scope of the claims. Applicant is advised to add the sequence disclosed in GenBank GI: 13365548 to the Sequence Listing. In this case, Applicant should submit a corrected Sequence Listing in compliance with 37 CFR 1.821-1.825, an amendment specifically directing entry of the corrected Sequence Listing into the application, a statement that the Sequence Listing provided for each of 37 CFR 1.821(c) and 1.821(e) are the same (37 CFR 1.821(f)), and a statement that the corrected Sequence Listing introduces no new matter (37 CFR 1.821(g)). In lieu of separate copies of the Sequence Listing as specified in 37 CFR 1.821(c) and (e), Applicant may file the Sequence Listing electronically via EFS-Web (http://www.uspto.gov/patents/ebc/index.jsp), in which case the statement under 37 CFR 1.821(f) is not required. Note that the statement under 37 CFR 1.821(g) is still required even if filed via EFS-Web.

Conclusion

It is expected that rectification of the issues presented above will place the application in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAMUEL C. WOOLWINE whose telephone number is (571)272-1144. The examiner can normally be reached on Mon-Fri 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Samuel Woolwine/
Examiner, Art Unit 1637